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SHARE
Sustainable Hand Applied Rehabilitation Equipments

A systematic review and Metanalysis

Dottorato in
Neuroscienze Clinico-Sperimentali e Psichiatria

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Contents

Abstract

Objectives. To systematically assess the clinical effectiveness, safety, patient-centred outcomes and potential environmental advantages of upper limb orthoses manufactured from bio-sustainable materials. **Methods.** Randomised controlled trials (RCTs) and non-controlled clinical trials (NCCTs) that reported at least one clinical or functional outcome for any bio-sustainable orthosis applied to upper limb were eligible. Five databases (CINAHL, PubMed, Web of Science, Scopus, ProQuest) were searched; reference lists were hand-searched. Risk of bias was assessed with RoB 2 (RCTs) and the NIH Quality-Assessment Tool (NCCTs). For continuous outcomes, pooled effects were calculated as Hedges' g or standardised mean change (random-effects DerSimonian–Laird model; Hartung–Knapp adjustment when $k \leq 2$); dichotomous outcomes were expressed as risk ratios. Heterogeneity (I^2, τ^2) and 95 % confidence intervals were reported. Leave-one-out analysis was performed when applicable. **Results.** Twelve studies (4 RCTs, 8 NCCTs; n = 498 participants, mean age 35.9 ± 24.5 years) met the inclusion criteria; six were suitable for quantitative synthesis. Risk of bias was low in one RCT, showed 'some concerns' in two, and high in one; no NCCT achieved a 'good' rating. Most green orthoses were wood-composites (76.3%), with the remainder additively manufactured by 3D-printing (23.7%); within the latter, polylactic acid (PLA) was the principal material (71.1%). Additive manufacturing was used predominantly for neurological disorders ($p<0.0001$). Neurological conditions accounted for 16% of all indications. Pooled analysis showed no statistically difference in upper limb functional improvement between bio-sustainable and conventional orthoses (SMD=0.05, 95%CI [-0.47–0.57], p=0.85, I^2=52%). A single-arm cohort study reported a moderate functional gain (SMC=0.61, SE 0.28, 95%CI [0.05-1.17],

p=0.029, I^2=0%). In post-stroke spasticity, bio-sustainable orthoses were associated with a higher probability of spasticity improvement (RR=2.69, 95%CI [1.66-4.36], p=0.0008, I^2=49%). Reduction in pain did not differ significantly between groups (SMD=0.46, 95%CI [-0.10–1.03], p=0.11, I^2=0%). Safety profiles were comparable (adverse event OR=1.31, 95%CI [0.72–2.37], p=0.60, I^2=60%). Overall patient satisfaction was not significantly different (SMD=0.06, 95%CI [-0.22–0.35], p=0.67, I^2=33%). **Discussion.** Quantitative syntheses indicate functional equivalence between biosustainable and conventional orthotic devices. Current evidence, albeit preliminary, indicates that orthoses manufactured from biosustainable materials are non inferior with regard to adverse events, analgesic efficacy and patient-reported satisfaction and may confer an additional therapeutic benefit in spasticity reduction and, to a lesser extent, hand function enhancement. Evidence is limited by small sample sizes, heterogeneous outcome reporting and methodological weakness, particularly in NCCTs. Robustly powered, prospective non-inferiority trials that incorporate standardised core outcome sets, extended follow up and embedded health-economic analyses are necessary to clarify long-term durability, environmental impact and cost-effectiveness. **Other.** Protocol registered in PROSPERO (CRD42024584327).

1. Introduction

A worldwide drive towards sustainability and responsible environmental management is crucial to face challenges such as climate change and to mitigate resource depletion. The growing recognition of the urgent need to adopt sustainable practices leads to a substantial shift towards “green” technologies and renewable resources in various sectors, including industry, energy and agriculture. Global efforts to promote sustainability is also supported by key regulatory bodies such as the U.S. Food and Drug Administrationo (FDA) and the European Medicines Agency (EMA). These organizations play a critical role in setting standards for the safety and efficacy of products, ensuring that green and sustainable alternatives meet rigorous scientific and environmental criteria. Their involvement is essential to promote innovation while safeguarding public health and promoting sustainable development across sectors, including pharmaceuticals and medical devices.

1.1 Traditional Orthotic Materials and Their Limitations

Orthoses, as defined by ISO 8549-1, are "externally applied devices to modify the structural or functional characteristics of the neuro-musculoskeletal system". They play a pivotal role in rehabilitation, providing support for weak or ineffective joints and muscles, correcting structural impairments and facilitating the restoration of functionality. Orthoses are classified into static, serial static, static progressive and dynamic depending on their therapeutic purpose. Static orthoses immobilize a joint or limb, providing stability, protection or positioning during healing; they are commonly used in the post-surgery period or in acute injury management. Serial static orthoses allow progressive stretching of soft tissues through repeated adjustments,

determining gradual improvement in range of motion (ROM). Static-progressive orthoses can deliver a constant force that elongates tissues improving joint positions over time, by using inelastic components, such as turnbuckles or Velcro straps. Dynamic orthoses incorporate elastic elements such as springs or rubber band to enable controlled movement, assist weakened muscles and promote functional movement patterns.

This diversity in orthotic designs ensures applicability across a wide spectrum of musculoskeletal and neurological conditions, ranging from fractures and ligament injuries to stroke rehabilitation and chronic deformities related to both orthopaedical and neurological conditions.

Historically, orthotic materials have been selected for their mechanical properties, ease of fabrication and durability. Common traditional materials include Plaster-of-Paris and fiberglass, which are valued for their rigidity and moldability and are widely used for immobilization; however, their weight and lack of breathability pose comfort challenges for long-term use[1]. Durable metals such as steel, aluminium and titanium are employed when high load-bearing capacity is required; although effective, their weight, production costs and environmental impact limit practicality in modern applications[2]. The introduction of thermoplastics (e.g., polypropylene, polyethylene) in the 1970s revolutionized orthotic production. These lightweight, moldable and non-toxic materials adapt to complex anatomical shapes and resist to boy fluid. Nevertheless, their environmental footprint remains significant due to energy-intensive production and non-biodegradability[1,3].

1.2 The Shift to Sustainable Materials

Researchers and manufacturers are exploring biodegradable polymers[4] and renewable composites that align with eco-friendly principles [5,5–8] to address the substantial environmental challenges associated with contemporary orthotic manufacturing. Early efforts focused on composites based on recyclable polymers combined to natural-organic fillers[9]. Among these, wood flour and fibres are the most widely used fillers[8], valued for their low cost, dimensional stability and relatively high elastic modulus: these attributes make them suitable for static or low-load orthotic applications[10]. Besides wood composites, other natural fibres used include flax, hemp, coir (coconut), jute and banana fibres[11]. Flax fibres provide high tensile strength and low weight and flax-based natural fibre composites (NFCs) have been explored for orthotic applications that require a balance between strength and flexibility; hemp fibres offer durability, low density and moisture resistance; coir fibres are abundant and possess good elasticity and toughness and when combined with biopolymers they provide improved shock absorption, making them ideal for orthotic pudding or cushioning; jute is inexpensive and renewable and its composites demonstrate excellent stiffness which makes them suitable for static orthoses; banana fibres are lightweight, strong and sustainable and they are increasingly being studied for orthoses that require flexibility[8,9].

Among polymer matrices, polylactic acid (PLA) has emerged as a leading contender[12,13]. Derived from renewable resources such as corn-starch or sugarcane, PLA is lightweight, rigid and fully biodegradable under industrial composting conditions, breaking down into non-toxic by-products such as water (H_2O) and carbon dioxide (CO_2)[4]. However, brittleness and moderate thermal resistance can limit its use in dynamic or high-stress applications[11]. Polycaprolactone (PCL) is another widely used biodegradable polymer, prized for its flexibility, low melting temperature and adaptability[14]. PCL conforms

closely to anatomical shapes, making it suitable for dynamic orthoses where comfort and adaptability are critical[15]. Its slow degradation rate ensures long-term stability, particularly in rehabilitation devices that require extended use[16].

Beyond NFCs, several other emerging materials have been reported. Thermoplastic elastomers are particularly suitable for dynamic orthoses and/or paediatric applications due to their stretchability and softness[3,17]. Moreover, bio-based polyurethanes, synthetised by plant oils, provide superior elasticity and durability and it determines its role in high-stress applications[18]. Recycled materials also contribute to sustainability initiatives: for instance, recycled polyethylene terephthalate (rPET) has been explored as an alternative to plastics and it could offer comparable mechanical properties (while reducing waste and carbon emissions significantly)[19,20]. Although rPET is not biodegradable, its reusability aligns with circular economy principles[21].

1.3 Advanced manufacturing: the role of 3D- and 4D-printing

The transition to sustainable materials is coupled with transformations in manufacturing. Additive manufacturing, including 3D- and 4D-printing, has revolutionised orthotic production by combining patient-specific customization with material efficiency and minimal waste[3,12]. 3D-printing techniques such as fused deposition modelling (FDM), selective laser sintering (SLS) and stereolithography (SLA)[22] produce orthoses with complex geometries tailored to the individual patient[2,23]. When integrated with advanced imaging methods (e.g. surface 3D scanning or magnetic resonance imaging, MRI), these techniques generate digital models that facilitate the fabrication of devices with precide patient-specific geometries[24,25]. Additive manufacturing also permits the incorporation of light-weight lattice or perforated structures that significantly reduce mass while preserving mechanical integrity[14,23]. Material versatility is a

further advantage: biodegradable polymers such as PLA and PCL can be extruded directly and reinforcement with natural fibres (e.g. jute, hemp) markedly elevates tensile strength and fatigue resistance, yielding devices comparable to those produced with conventional methods[3,16]. Because material is deposited only where required, additive manufacturing minimises the off-cut waste typical of subtractive processes[26].

4D-printing extended these benefits by introducing stimuli-responsive materials[3], such as shape-memory polymers, that enable the orthosis to adjust stiffness or geometry in response to temperature, moisture or mechanical loading[3,27]. Although still in the experimental stage, 4D-printing techniques hold significant potential for creating orthoses that can evolve with the patient's rehabilitation stage, reducing the need of manual adjustments and offering an entirely new level of functionality and convenience[27].

1.4 Clinical benefits of green orthoses

Sustainable orthoses provide several patient-centred advantages over traditional materials. Precise digital modelling ensures an optimal fit and distributes pressure evenly across the sking, enhancing comfort and reducing the risk of pressure sores during prolonged wear[23,28]. Lighweight lattice or perforated architectures decrease overall mass, improve ventilation and limit heat-moisture accumulation[3,25], sustaining adherence in long-term rehabilitation and individuals with active lifestyles[2,29]. Reduced mass decreases muscular fatigue; together, these factors enhance patient satisfaction and adherence, translating into longer wear times[1] and better clinical outcomes[2,29].

Beyond individual benefits, environmentally sustainable devices reduce the healthcare sector's carbon footprint[26].

2. Aim of the study

The principal aim of this systematic review is to evaluate the clinical effectiveness and reliability of bio-sustainable materials employed in upper limb orthoses and to determine their advantages and limitations comparing their clinical performance with that of conventional materials.

Primary outcomes include hand function improvement, spasticity control, pain reduction, adverse events, together with patient-centred metrics such as comfort and satisfaction. Secondary analyses will aim to quantify the environmental and economic sustainability of these materials.

The resulting body of evidence will guide clinicians and investigators to follow a more sustainable and effective upper limb rehabilitation solutions across diverse patient populations and healthcare settings.

3. Methods

3.1 Protocol and registration

The reporting of this systematic review was guided by the standards of the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA)[30]. The protocol was prospectively registered in the PROSPERO database (#CRD42024584327) and it is publicly available at the following link: https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=584327.

3.2 Eligibility criteria

Peer-reviewed and published as full-text articles, written in English or Italian, were eligible for this systematic review.

Acceptable study designs comprised randomised controlled clinical trials (RCTs) and non-controlled clinical trials (NCCTs) that evaluated bio-sustainable upper limb orthoses and reported at least data on one clinical or functional outcome. Systematic reviews, meta-analyses, conference abstracts and studies lacking sufficient methodology or outcome data were excluded.

3.3 Literature search strategy and selection process

Five major electronic databases (CINAHL, PubMed, Web of Science, Scopus and ProQuest) were searched from inception to 1 July 2024 to identify studies relevant on sustainable upper limb orthoses. The search strategy combined terms referring to eco-friendly materials (“biocompostable,” “biodegradable,” “sustainable,” “eco friendly,” “vegan”) with terms describing orthotic devices (“braces,” “splints,” “orthosis”). Boolean operators “OR” within and “AND” between blocks were applied. Reference lists of all included studies and relevant reviews were hand-searched for additional citations.

Records identified through search strategy and citation chaining were imported into Rayyan[31] and duplicates removed. The remaining records were screened at the title and abstract level, categorizing them as “excluded”, “maybe” and “included”. The latter two underwent to a full-text appraisal to confirm their eligibility and inclusion in the review. Reasons for exclusion were recorded.

The process was conducted in accordance with established guidelines for systematic reviews, ensuring a thorough and unbiased selection of studies.

3.4 Extraction data

A piloted extraction form captured studies characteristics (study title, lead authors, year of publication, country, study design), ensuring clear identification and contextualization of each study within the broader scientific literature. Participant characteristics (age, sex, clinical indication for orthotic use), intervention protocols (type of device, orthotic materials and, when applicable, its customization techniques, wear time) were specified; conventional technologies and/or materials were collected when comparators were present. Primary and secondary outcomes of the studies were collected. Statistical measures, including means ± standard deviation (SD), medians ± interquartile range (IQR), confidence intervals (CI) and reported or calculated p-values, were systematically extracted. Missing data were derived, where possible, from CIs or other information provided. All data were systematically collected using standardized tables to ensure accuracy and consistency. These items provided the foundation for both qualitative and quantitative analyses, leading to an integrated evaluation of the effectiveness and sustainability of innovative orthoses.

3.5 Risk-of-bias assessments

A comprehensive risk-of-bias assessment was implemented to ensure that conclusions of the systematic review and meta-analysis are anchored in a transparent and methodologically rigorous appraisal of study quality.

Methodological quality was appraised using two distinct tools, based on the study design.

The Cochrane Risk of Bias 2 (RoB 2)[32] tool was used for the evaluation of the RCTs: it assesses bias across five domains, i.e. (1) randomization process, (2) deviations from intended interventions, (3) missing outcome data, (4) measurement of the outcome and (5) selection of the reported results. Each study was classified as "low risk", "some concerns" or "high risk", according to the overall judgment derived from these domains.

The NIH Quality Assessment Tool[33] was applied for non-controlled studies: it evaluates study quality based on criteria such as study objective clarity, eligibility criteria, sample size justification, outcome measurement reliability, statistical analysis appropriateness and completeness of follow-up. Each study was rated as "good", "fair" or "poor" quality according to the predefined criteria of the NIH tool.

Risk of bias was assessed by the author and any doubts were resolved through discussion with a second and, when necessary, a third reviewer. Summary tables were compiled to present each study's risk of bias judgments, offering an overview of methodological quality and enabling clear comparisons of study reliability. The findings were also represented in figures to facilitate interpretation.

3.6 Data synthesis and statistical analysis

A narrative synthesis of the findings of the included studies was provided, structured around each outcome. For each outcome, studies were selected by comparing the intervention characteristics. The groups and key outcomes were then summarised in tables and graphics.

Quantitative synthesis followed a hierarchical strategy that depended on study design and outcome. Before pooling, scores expressed on different ranges were linearly rescaled to a common metric.

A traditional between-group metanalysis was made if at least two studies reported the same outcome alongside a concurrent control arm. For continuous outcome, weighted mean difference (MD) was calculated when studies employed a common measurement scale; otherwise, the standardised mean difference (SMD) was computed using Hedges' g, which applies a small sample bias correction. Dichotomous outcomes were pooled as risk ratio (RR), odds ratio (OR) and risk difference (RD), applying a 0.5 continuity correction for zero-cell counts. Pooled estimates were generated with a DerSimonian–Laird random-effects model to accommodate the anticipated clinical heterogeneity; when only two studies contributed, the Hartung–Knapp–Sidik–Jonkman adjustment was implemented.

When studies presented only within-group data, a pre-post metanalysis was carried out. The standardised mean change (SMC) and the standardised mean change with change score (SMCC) were derived, assuming a within-person correlation (ϱ) of 0.5 and exploring 0.3-0.8 in sensitivity analyses.

95 % CI were reported to depict the dispersion of true effects across future settings.

For both syntheses, statistical heterogeneity was quantified with Cochran's Q, I^2 and the Paule–Mandel τ^2 estimator. Leave-one-out analyses assessed the influence of individual studies.

No formal adjustment for multiple testing was applied because every analysis corresponded to a pre-specified hypothesis. Statistical significance was set at a p-value < 0.05.

All analyses were performed using R Statistical Software (version 4.4.2; R Core Team 2024)[34] with the meta, metafor and dmetar packages. Graphical outputs were created with ggplot2.

4. Results

4.1 Studies selection process

A total of 6210 papers were initially identified from the electronic searches. After automatic and manual removal of 332 duplicate records, 5878 references remained for screening. Title- and abstract-level screening excluded 5854 articles. An further 12 full-text reports were excluded owing to inappropriate study design or an insufficient description of the orthotic material. Consequently, 12 studies met the inclusion criteria for qualitative synthesis (Chae et al., 2020[35]; Chang et al., 2018[36]; Gwilym et al., 2020[37]; Lindsfor and Salo, 2012[38]; Lindsfor and Salo, 2014[39]; Martynov et al., 2020[40]; Portnova et al., 2018[41]; van der Stelt et al., 2020[42]; Waldburger et al., 2021[43]; Wang et al., 2018[44]; Yoo et al., 2019[45]; Zheng et al., 2020[46]). Six of these studies were further eligible for quantitative synthesis (Chae et al, 2020; Gwylm et al., 2020; Martynov et al., 2020; Waldburger et al., 2021; Wang et al, 2018; Zheng et al., 2020). The selection process is illustrated in the PRISMA flow diagram (*Figure 1).*

4.2 Study characteristics

The designs of the included studies were heterogeneous. Four studies were RCTs (Gwilym et al, 2020; Martynov et al, 2020; Waldburger et al, 2021; Zheng et al, 2020), whereas the remaining eight studies were NCCTs (Chae et al., 2020; Chang et al., 2018; Lindsfor and Salo, 2012; Lindsfor and Salo, 2014; Portnova et al., 2018; van der Stelt et al., 2020; Wang et al., 2018; Yoo et al., 2019).

Across all studies, a cumulative total of 498 participants were enrolled. The sample size of individual RCTs ranged from 24 to 170 participants, whereas the NCCTs enrolled between 1 (single-case experimental case report) to 67 patients. The mean cohort size was 41.3±53.1 (median=21, IQR 5.5-53.5). Females

represented 40.2 % of the pooled sample (n=200). The weighted mean age was 35.9 ± 24.5 years; paediatric participants were included only in the RCT by Martynov (2020). Clinical indications were predominantly orthopaedic (84.3% of the entire cohort, n=420; excluding controls, it represented the 81.9% of cases, n=191). Neurological indications accounted for 16.0% of all cases (n=74) and for 23.1% when only the experimental arm was considered. Chronic post-stroke hemiparesis constituted 79.7% of the neurological subgroup (n=59), cervical spintal cord injury 17.6% (n=13) and peripheral nerve injury 2.7% (n=2). Four patients (0.8%) received orthoses after skin-graft surgery. The recruitment windows varied from two weeks to several decades after the index event.

Regarding materials, two orthotic technology families were identified. Thermoformable wood composites were used in 244 experimental-arm participants (76.3%), whereas additively manufactured biopolymers were used in the remaining 76 cases (23.7%). Among the latter, PLA was used to fabricate 54 devices (71.1%), bio-thermoplastic polyurethane[47] (bio-TPU) 2 (2.6%) and light-activated resins 20 (26.3%). The use of additively manufacturing was prevalent in neurological disorders ($p<0.0001$). Several devices incorporated bespoke straps, soft padding, four-bar linkages or ratchet mechanisms to amplify grasp

Outcome domains and metrics were heterogeneous. Patient satisfaction measures appeared in 10/12 trials (83.3%) and it was measured with Quebec User Evaluation of Satisfaction with assistive Technology 2.0 (QUEST, n=3), 5- or 10-point Likert scales (n=4) or study-specific questionnaires (n=3). Hand function improvement was assessed in 7/12 studies (58.3%) using the Jebsen-Taylor Hand Function Test (JHFT, n=2), Fugl-Meyer Assessment (FMA, n=2), Toronto Rehabilitation Institute Hand Function Test (TRI-HFT, n=1), Box-and-

Blocks test (BBT, n=1) or a three-jaw-chuck grasp dynamometry (n=1). Adverse events were explicitly reported in 6/12 studies (50.0%). Pain reduction outcomes were analysed in 4/12 investigations (33.3%) using Visual Analogue Scale (VAS) in 75.0% of cases (n=3) or EuroQol 5-Dimension Visual Analogue Scale (EQ-5D VAS) in 25.0% (n=1). Spasticity reduction, mechanical stiffness and passive range of motion (PROM) were each investigated in 2/12 studies (16.7%, each). Spasticity was assessed with the Modified Ashworth Scale (MAS). Stiffness was recorded instrumentally as functional stiffness (N/mm) or low-frequency elastic modulus (N/mm²). PROM with conventional goniometric PROM metrics. *Table 1* summarises the principal characteristics and results of all included studies.

4.3 Risk of bias

Among RCTs, one study (Zheng et al, 2020) was judged as "low risk", two (Gwilym et al, 2020; Martynov et al, 2020) presented "some concerns" and one (Waldburger et al, 2021) exhibited "high risk" of bias. Methodological strengths included adequate random sequence generation and allocation concealment in three trials (Gwilym et al, 2020; Martynov et al, 2020; Zheng et al, 2020) coupled with low or balanced attrition. Blinding was rarely feasible: indeed, three trials (Gwilym et al, 2020; Martynov et al, 2020; Waldburger et al, 2021) were open-label and also relied partly or entirely on participant reported outcomes, introducing the risk of performance and detection bias. Selective-reporting concerns were noted in all but one (Zheng et al, 2021) RCTs, related to the absence of publicly available protocols or clearly predefined primary endpoints. *Table 2* provide the detailed RoB2 assessment, visually summarized in *Figure 2*.

None of the NCCTs reached a "good" rating. Only four studies (Lindsfors and Salo, 2012; Lindsfors and Salo, 2014; Wang et al, 2016; Yoon et al, 2019) were rated "fair". Common deficits were extremely small samples, lack of sample

size justification, unblinded outcome assessment, limited follow-up information and inadequate adjustment for confounding. Although most authors described the intervention and type of orthosis in an adequate technical detail and captured pre- versus post-intervention data, the internal validity of the findings is little. *Table 3* explicitly lists the specific item ratings of NIH Quality Assessment and *Figure 3* visually summarized it.

4.4 Syntheses of outcomes

Results are first described narratively, followed by quantitative syntheses where appropriate.

4.4.1 Hand functionality improvement

Wang et al 2018 fabricated custom-made PLA fingerboards for 18 in-patients with subacute post-stroke hand spasticity. The Grip-Strength-Index (GSI, expressed as kg/kgx100) increased non significantly from baseline to the three-weeks and three-months follow-up (respectively, 0.018±0.041 – 0.025±0.054 – 0.032±0.067). The mean Brunnström hand stage improved (mean ± SD: 2.77±0.80 vs 3.31±0.77, $p<0.05$) and MAS decreased (2.38±0.63 vs 1.73±0.69, $p<0.05$).

Yoo et al 2019 tested a 3D-printed myoelectrical wrist-driven orthosis (WDO) in 10 individuals with a diagnosis of cervical spinal cord injury (SCI). The TRI-HFT score increased from 29.4 to 45.0 points (Part I) and from 26.8 to 47.6 (Part II), both $p<0.01$.

Portnova et al 2018 treated three patients with cervical SCI with 3D-printed PLA WDOs. They reported that JHFT completion time decreased by 1.3 sec and 61.9 sec in two participants, while BBT increased by 4 and 3 blocks, respectively; three-jaw-chuck forces rose by 122.2% and 13.3%, whereas one participant managed to execute grasp (previously unable to perform the movement).

Zheng et al 2020 compared a light-cured resin wrist–hand orthosis (WHO) with a conventional low-temperature thermoplastic plate in 40 hemiparetic stroke survivors. Over 6 weeks, the experimental group gained +1.3-point increment on the upper-limb section of FMA, whereas the control group improved +0.2 points ($p < 0.001$). No other hand-specific scales were employed.

Chae et al 2020 applied a bio-TPU WHO in two neuropathic cases, with a mean JHFT aggregate scores increased modestly (11.56±2.32 to 12.12±2.70) and dynamometer-measured grasp power rising by 38 % and 50 %.

An anectodical single-subject experiment (Chang et al 2018) documented a 4-point upper limb section of FMA increase (15→19) in a single post-stroke case treated with 3D-printed PLA innovative orthosis for phalanx extension neurofacilitation (iOPEN).

Outside neurorehabilitation, Gwilym et al 2020 randomised 120 adults with distal radius fractures to wood-composite or fibreglass static orthoses (casts). Patient-Rated Wrist Evaluation (PRWE) function subscales (0-50 points) were 15±12 (experimental group) versus 13±22 (control group) with no statistically significant difference.

Meta-analysis

A random-effects meta-analysis pooling the eligible trials (Gwilym et al, 2020 and Zheng et al, 2020) was done. PRWE-function scale scores were multiplied by -1 before SMD was computed to align the orientation of the scale. Hedges'g =0.05 (95%CI [-0.47–0.57], p=0.85) was calculated starting from Gwilym's SMD=--0.17 (95%CI [-0.56–0.23]) and Zheng's SMD=0.38 (95%CI [-0.25–1.01]) (Figure 4). Heterogeneity was moderate ($Q = 2.08$, $df = 1$, $p = 0.15$; $I^2 = 52\ \%$; $\tau^2 = 0.08$), reflecting some variability in treatment effects that could not be attributed to sampling error alone

A supplementary pre-post synthesis of the two single-arm series (Chae et al, 2019 and Wang et al) was done. Using the conventional pre-post correlation of ϱ=0.50, Chae's splint users achieved an SMC=0.13 (SE 0.71, 95%CI [-1.26–1.52], p=0.85), whereas Wang's wood-composite group SMC=0.70 (SE 0.31, 95%CI [0.09–1.31], p=0.024). Pooling together using random-effect metanalysis, SMC=0.61 (SE 0.28, 95%CI [0.05–1.17], p=0.029 (*Figure 5*). If Hartung-Knapp correction is applied (considering the small sample size), SMC=0.61 (95%CI [-0.77–1.99], p=0.11). Heterogeneity study revealed Q=0.54, df=1, p=0.46, τ^2=0 and I^2=0%.

4.4.2 Reduction in spasticity

One RCT (Zheng et al, 2020) and one NCCT (Wang et al, 2018) evaluated upper limb spasticity outcomes (both studies used 3D-printed orthoses).

In Zheng's trial (n=40), patients wore their WHO for 4-8 h/day over six weeks. Baseline MAS scores were 2 or 3 in 100% of patients: indeed, 65 % of the experimental group and 70 % of controls were rated MAS 2, whereas the remaining were rated MAS 3. After three weeks, a ≥ 1-grade MAS reduction was observed in 10% of experimental group and 25% of controls (p=0.496). At six weeks, 65% of cases achieved MAS relief (55% 1-grade and 10% 2-grade improvement) compared with 30% of controls (1-grade shift), p=0.02.

Moreover, mean passive wrist-extension increased by 10.3±3.8° in the experimental arm versus 3.3±2.9° in controls (Z=6.52, p<0.001). Concordantly, the upper limb FMA subscores increased 1.3±1.0 points (3.9 ± 2.3 to 5.2 ± 2.4) in the first group versus 0.2±0.3 points in controls (p<0.001).

Wang's three-month series (n=18) reported a MAS shift from 2-4 at baseline to ≤ 2-grade in 85% of wrist by month three of a daily wear (mean 4.54±2.60 h/day) of fingerboard (p<0.05)

As mentioned before, a single-case report (Chang et al., 2018) described a 4-point upper limb FMA subscore gain, attributing improvement to "suppressed flexor spasticity", though MAS data were not provided.

Meta-analysis

A single-arm responder meta-analysis was performed (Figure 6). Responders were defined as participants achieving ≥ 1-grade MAS reduction from baseline to final follow-up. For Zheng et al, 2020, RR was calculated comparing the biodegradable splint with the conventional thermoplastic control; for Wang's case series, the responder proportion was contrasted with the external conventional control from Zheng. Biodegradable splints yielded 26/33 responders (79%), whereas the conventional splints produced 6/20 responders (30%). The study-specific RRs were 2.17 (95% CI[1.03–4.55], p=0.04) for Zheng and 3.15 (95%CI [1.67–5.95], p=0.01) for Wang versus the external control. Pooled analysis (random effects) showed a combined RR=2.69 (95% CI[1.66–4.36], p=0.008) with moderate heterogeneity (I^2 = 49 %, Q=1.96, p=0.16).

4.4.3 Reduction in pain

Four studies assessed pain-specific outcomes (Chae et al, 2020; Gwilym et al, 2018; Wang et al, 2018; Zheng et al, 2020).

In the Gwilym RCT (n=120), mean PRWE pain subscores at six weeks were 15±10 in the experimental group versus 16±12 in controls, with weekly VAS curves essentially overlapping. Zheng's RCT detected no inter- and between-group VAS difference (Δ VAS scores = 0 at six weeks, p=0.637).

Two small cohorts reported within-group VAS decreases. Chae's NCCT revealed decreased VAS score in both patients (-4 and -2 points, respectively). Wang's group described a drop in VAS mean between baseline, after three-

weeks and after three-months follow up (2.00±1.58 versus 1.85±1.34 versus 1.69±1.03).

Meta-analysis

Two RCT contributed to a fixed-effect model (n=160, Gwilym et al, 2020; Zheng et al, 2020). Zheng et al reported MD=+0.29 (95%CI [-0.57–1.15], p=0.51) in favour of controls; Gwilym et al showed MD=+0.60 (95%CI [-0.16–1.36], p=0.12). The pooled SMD was +0.46 (95%CI [-0.10–1.03], p=0.11). Statistical heterogeneity were Q=0.28, df=1, p=0.60, I^2 = 0 % (*Figure 7*).

A pre-post synthesis of four single-arm data sets (Chae et al, 2019; Gwilym et al, 2020; Wang et al, 2018; Zheng et al, 2020) was analysed. Assuming ϱ=0.50, each group's change in pain was standardised. The study-level effect sizes were SMC=-0.22 (95%CI [-0.69–0.25], p=0.38) for Wang, SMC=0.22 (95%CI [-0.22–0.66], p=0.35) for Zheng, SMC=-4.23 (95%CI [-8.60–0.14], p=0.17) for Chae and SMC=-0.23 (95%CI [-0.51–0.05], p=0.13) for Gwilym. Pooled SMC was -0.12 (95%CI [-0.49–0.25], p=0.50). Statistical heterogeneity was Q=6.41, df=3, p=0.09, I^2=53.3%, τ=0.42. (Figure 8).

Sensitivity analyses with ϱ = 0.30 and ϱ = 0.80 were concordant (-0.11 (95%CI [-0.35–0.14], p=0.39), τ^2=0.01, I^2=16 % and -0.15 (95%CI [-0.60–0.30], p=0.51), τ^2=0.11, I^2=65%).

4.4.4 Impact of adverse events

Six studies (three RCTs and three NCCTs) recorded device-related complications.

In Martynov RCT (n=170), breakage rates were 3.6% (95%CI [0.7–10.2]) vs 3.5% (95%CI [0.7–9.0]) between arms (p>0.999). Overall adverse events incidence (pain, paraesthesia, pressure injuries, disturbance of sensation) was 25.0% in the experimental group (n=21/84) and 27.9% in controls (p=0.720), with no serious

events or orthoses-related infections observed. Gwilym et al reported 8/120 cases of minor complications (7/60 in experimental and 1/60 in control groups, p=0.06), mostly skin irritation (5/7 in the experimental arm and 1/1 in the control group, p>0.999) and breakage or comfort-related changing (1/7 each in the cases). No patient in either group experienced neurovascular compromise, infection or material allergy or other serious adverse events. Waldburger et al observed partial material fissures without replacement in 30% of cases (n=3); self-reported strong pain was noted in a single case (10%) in the experimental arm. No pressure sores, skin breakdown or allergic reaction were recorded. Lindsfors and Salo (2014) documented a single case of material fracture (1/67) and discomfort-related orthosis replacement in 9/67 recipients (13.4%). Minor advers events were registered, such as compression or rubbing (n=9/56, 16.1%) and bad odour (n=11/56, 19.6%). In Wang's prospective cohort, it was reported transient mild oedema, judged clinically insignificant, in 5/13 (38.5%) subjects after a three week period, reduced to 3/13 (23.1%) subjects after the three-months entire period of observation. Van der Stelt et al's 3-month programme do not report any adverse events (n=0/4).

Meta-analysis

Across the three RCTs (Martynov et al, 2020; Gwilym et al, 2020; Waldburger et al, 2021, n=314), 19.6% of intervention participants and 16.0% of controls experience at least one adverse event.

Mantel–Haenszel pooling showed OR=1.31 (95% CI [0.72–2.37]; p=0.60), RR=1.05 (95% CI [0.65–1.70]; p=0.83) and RD=0.071 (95% CI [0.001–0.141]; p=0.047) (*Figure 9*). Between-study heterogeneity was moderate (Q = 4.99, df = 2, p=0.08; I^2 =59.9 %, τ^2=1.25).

Leave-one-out analysis showed that removing Martynov yielded OR=7.31 (95% CI [1.27–42.08]; p=0.026) and RD=0.110 (95% CI [0.027–0.192]; p=0.009), removing Waldburger produced OR=1.06 (95% CI [0.55–2.03]; p=0.87) and RD=0.061 (95% CI [-0.012–0.134]; p=0.10), while removing Gwilym resulted OR=0.95 (95% CI [0.49–1.84]; p=0.87) and RD=0.019 (95% CI [−0.097–0.136]; p=0.74), indicating robust OR and RR estimates but unstable RD.

4.4.5 Patient satisfaction

User-reported comfort with bio-derived or additively-manufactured orthoses is consistently high in the NCCTs and statistically non inferior to conventional materials in RCTs.

Meta-analysis

All four RCT included in this systematic review (Gwilym et al, 2020; Martynov et al, 2020; Waldburger et al, 2021; Zheng et al, 2020) compared patient satisfaction between bio-derived and standard materials. Different scales were used, so each result was harmonised so that higher scores consistently represent greater satisfaction (in particular, Martynov et al used a 5-point Likert scale reversed in direction because lower scores indicated better perceptions).

Random-effects pooling produced g=+0.06, (SE=0.15, 95% CI [-0.22–0.35]; p=0.67). Heterogeneity was moderate (Q = 4.45, df = 3, p = 0.22; I^2 = 32.6 %, τ^2 = 0.028) (*Figure 10*).

Leave-one-out sensitivity analysis showed that removing any single trial shifted the pooled estimate only within a narrow band from g =-0.05 to g =+0.13, never approaching statistical significance, underscoring the internal robustness of the findings.

4.4.6 Environmental and economical sustainability

None of the included studies reported quantitative data on life-cycle environmental metrics or cost-effectiveness, precluding any formal analysis.

5. Discussion

This is the first systematic review about the impact of bio-derived orthoses in clinical outcomes across rehabilitation. Twelve primary studies, including four RCTs, were eligible, but the cumulative sample remained modest (n=498) and methods were heterogenous. Despite these constraints, two consistent themes emerged: bio-derived and/or 3D-printed bio-based orthoses match, and occasionally exceed, the clinical performance of conventional materials; moreover, their safety profile and user acceptance are at least equivalent.

The clearest signal came from antispastic outcomes. Both Zheng's RCT and Wang's prospective series reported two- to three-fold higher responder rates than thermoplastic comparators, sustained throughout the follow up period. The pooled risk ratio (RR=2.69) suggests a clinically important effect, although based on only 58 participants. Notably, gains in passive extension and modest FMA motor improvements hint a neuro-plastic rather than purely mechanical effects.

When analysing the improvement of hand function, the trajectories of the studies is reassuringly consistent with functional gain, even if effect sizes varied by diagnosis and splint type. In neuro-rehabilitation cohorts, improvements were clinically tangible. Wang's orthoses, for example, moved patients almost an entire Brunnström stage in the first three weeks with further gains after three months; the concurrent MAS score decrease (-0.65 points) indicated that the improved hand control was not simply a masked spasticity but it is genuine recovery of movement, indicating a shift from gross mass-flexion to emerging voluntary extension. Yoo's myolectric orthosis produced even larger effects, showing an augmentation of the TRI-HFT scores of 15-21 points, translating into meaningful improvements in self-care activities and new independence as

reflected in FIM subscores. Single-arm data reinforce improvement in hand function of bio-orthoses with a combined SMC=0.61 (95%CI [0.05-1.17], p=0.029), although the results derived from a small sample size (n=15). When RCTs were considered, the direction of benefit is broadly the same, albeit more modest. When Gwilym and Zheng were pooled, the SMD centred on the null, yet the confidence interval remained wide and moderate heterogeneity suggest a clinically relevant difference that larger trials could unmask. Taken together, these data suggest that the effect magnitude is diagnosis-specific (larger in dynamic neuro-motor conditions, smaller in conditions that required static orthoses), while precision is presently inadequate for firm inferences.

Pain relief remains largely unchanged. Meta-analyses point clearly that bio-orthoses do not exacerbate nociception, although they do not confer a systematic analgesic advantage beyond that achieved in control groups: indeed, Gwilym and Zheng show a pooled SMD=-0.12 (p=0.50). The finding is reassuring in terms of non-inferiority, yet it also underscores that design innovation alone does not guarantee pain relief; targeted biomechanical or neuro-modulatory features may be required. Notably, different results emerge when neuropathic pain is considered: in Chae's cases, VAS markedly dropped but, because of the small sample size, no statistical test was done. These improvements should be interpreted as proof-of-concept that precise positioning and gentle load sharing can reduce nociceptive or compressive pain, rather than as effect sizes that can be generalised beyond this single-arm meta-analysis.

In terms of safety and acceptability, adverse event rates were low and comparable (19.6% versus 16.0%). Events were overwhelmingly minor, such as skin irritation, hairline material cracks, transient oedema, with no serious neurovascular compromise or infection reported. Patient-reported satisfaction

was consistently high; the pooled effect (g=0.06) confirmed equivalence. Qualitative comments highlighted perceived advantages in lightness, breathability and aesthetics, counter-balanced by occasional concerns about rigidity of PLA or odour with wood-composite orthoses.

Surprisingly, none of the included studies quantified life-cycle impacts or cost-effectiveness Preliminary costing from two trials indicates per-device material expenses of 10-25 USD for FDM-printed orthoses, cheaper than thermoplastic comparators. Future trials should incorporate standardised cradle-to-grave analyses and micro-costing to substantiate the frequently cited sustainability claims.

6. Study limitations

Several methodological limitations need to be considered when analysing the results of this systematic review. First, the concept of a biodegradable or additive manufactured orthosis is emergent, so it raises a concrete risk of publication bias, as early adopters may preferentially disseminate positive findings. Moreover, sequence generation and allocation concealment were rarely reported; blinding of participants, clinicians and therapists was largely infeasible and withdrawals were often handled per-protocol without detailed accounting of attrition, thereby permitting selection, performance and detection bias.

Statistical reliability is further weakened by very small sample sizes (frequently fewer than 20 participants per arm) and by the substantial contribution of NCCTs, which reduce power and preclude robust causal inference.

Clinical and methodological heterogeneity is also present. Study populations present varied diagnoses and recovery phases. Orthotic designs ranged from passive positioning orthoses to actively powered exoskeletons. Wearing schedules and training protocols differed markedly. Follow-up rarely extended beyond three months, leaving the durability of observed benefits unverified. Outcome assessment often lacked uniformity and scale conversions (that is done to facilitate pooling) may have introduced additional measurement error.

In conclusion, no study triangulated tone measures with electromyography or elastography to univocally quantify the results. None of the studies systematically evaluated cost, fabrication time or post-wear persistence of effect: these parameters are pivotal for real-world implementation but lie outside the reported clinical endpoints.

7. Conclusion

The present review remarks that upper limb orthotic care is undergoing towards an ecological evolution without overlooking clinical cornerstones. The adoption of sustainable materials provides a promising alternative to traditional synthetic splints, offering advantages such as biodegradability and reduced environmental footprint, even if it is not yet fully quantified. Studies consistently indicate that bio-based orthoses are non inferior to traditional materials, without compromising structural integrity or therapeutical benefits. Indeed, outcomes vary across different pathologies, even if the overall trend remained positive. Spasticity and hand function improved with bio-based orthoses in neurological conditions and antispastic effect seems to be superior than conventional orthoses.

Nevertheless, these preliminary findings need to be interpreted with caution because clear research gaps persist around long term outcomes, the lack of objective biomechanical metrics and adequately powered RCTs. Further studies are needed to confirm these data and to consider bio-based materials in upper limb orthotic care.

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Tables

First author, year (country)	*Study design*	*Subject N (I, C)*	*Diagnosis*	*Intervention and comparator orthosis type (and wearing time) Material of customization*	*Baseline and follow up*	*Outcomes*	*Method*	*Main results*
Chae et al., 2020 (South Korea)	Before-&-After study (NCCT)	2 I	Carpal (1) and ulnar (1) neuropathy	Static radial 3D-printed WHO (2 weeks); Static semi-circular 3D-printed WHO (8 weeks) *Bio-TPU*	T1: 1) 2 weeks 2) 8 weeks	Improvement in hand function	JHFT Grasp & pinch power	↑ 11.56 ± 2.32 → 12.12 ± 2.7; Grasp ↑ (+38 % & +50 %); Pinches ↓
						Reduction in pain	VAS	↓ 6.5 ± 0.71 → 3.5 ± 0.71
						Patient satisfaction	QUEST 2.0	4.35 ± 0.38
Chang et al., 2018 (Taiwan)	Before-&-After study (NCCT)	1 I	Post-stroke hemiparesis	Dynamic dorsal 3D-printed WHFO (1 month) *PLA*	T1: 1 month	Improvement in hand function	FMA	↑ 15 → 19
Gwilym et al., 2020 (UK)	RCT	60 I 60 C	Distal radial fracture	Static circular WHO (3 months) I: *Wood-composite* C: *Fiberglass*	T1: 1 week T2: 5 weeks (±14 days) T3: 3 months (±3 weeks)	Improvement in hand function	PRWE	↑ PRWE in both groups
						Reduction in pain	EQ-5D VAS	↓ in both groups
						Patient satisfaction	EQ-5D-5L	↓ in both groups
						Adverse events	Number of events	7/60 (EA) vs 1/60 (CG), n.s.
Lindsfors & Salo, 2012 (Finland)	Prospective study (NCCT)	33 I	Distal radial fracture	Static circular WHO (4.2 weeks) *Wood-composite*	T1: 1-6 weeks	Adverse events	Number of events	10/27 (negligible skin irritation)
						Patient satisfaction	Qualitative	Rated “high” for all patients

(continue)

First author, year (country)	*Study design*	*Subject N (I, C)*	*Diagnosis*	*Intervention and comparator orthosis type (and wearing time) Material of customization*	*Baseline and follow up*	*Outcomes*	*Method*	*Main results*
Lindsfors & Salo, 2014 (Finland)	Prospective study (NCCT)	67 I	Carpo-metacarpal OA (41) Thumb UCL rupture (12) Scaphoid pseudoarthrosis (6) Thumb metacarpal instability (3) Thumb tendon transection (3) Thumb fractures (2)	Static circular WHO (1-10 weeks) *Wood-composite* *[Cast-1: Woodcast 2 mm + Ribbon* *Cast-2: Woodcast Soft + Ribbon]*	T1: 1-10 weeks	Stress stability Patient satisfaction Adverse events	Functional stiffness (N/mm) Questionnaires Number of events	Woodcast 2 mm: 9.7 ± 0.5; Soft 1 mm: 1.0 ± 0.3; Ribbon: 1.9 ± 0.2 "Very comfortable": 15/26 (Cast-1); 20/30 (Cast-2) Compression/discomfort: 9/67; Bad odour: 11/67
Martynov et al., 2020 (Germany)	RCT	84 I 86 C	Upper-limb fracture	Static circular WHO (1 month) I: *Wood-composite* C: *Fiberglass + PP padding*	T1: 1 day T2: 5 days T3: 10 days T4: 14 days T5: 21 days T6: 28 days	Stress stability Patient satisfaction Adverse events	LFEM (N/mm²) 5-point Likert scale Number of events	13.07 ± 0.79 (heated EA) vs 15.37 ± 1.37 (CG), $p < 0.001$ 1.22 ± 0.25 vs 1.34 ± 0.6, ns 21/84 (25 %) vs 24/86 (27 %), ns
Portnova et al., 2018 (USA)	Prospective study (NCCT)	3 I	Cervical spinal-cord injury (chronic)	Dynamic wrist driven dorsal 3D-printed WHFO (10 min) *PLA* C: Non-use of orthosis	T1: 2nd visit T2: 3rd visit	Improvement in hand function Patient satisfaction	JHFT Box-and-Blocks 3-jaw-chuck grasp 10-point scale	↓1.3 s (1 pt);↑ 61.9 & 10 s (2 pts); Box-and-Blocks: +4 & +3 ↑ Grasp for all patients (+122.2%, + 13.3%, grasp for the first time) Function 6.8; Aesthetics 7.7; Comfort 7.7

(continue)

First author, year (country)	*Study design*	*Subject N (I, C)*	*Diagnosis*	*Intervention and comparator orthosis type (and wearing time) Material of customization*	*Baseline and follow up*	*Outcomes*	*Method*	*Main results*
van der Stelt et al., 2020 (Netherlands, Sierra Leone)	Prospective study (NCCT)	8 I	Upper-limb amputation (4) Skin transplantation (4)	Upper limb prostheses (≥4 hours for 3-4 weeks) *PLA*	T1: 4 weeks	Patient satisfaction Adverse events	Questionnaires Number of events	More confidence, some functional gains (2/4) 0/4
Waldburger et al., 2021 (Switzerland)	RCT	14 I 10 C	Post-traumatic hand surgery (± chronic pain)	Metacarpal 3D-printed brace (35.1 days) I: *PLA* C: *Thermoplastics* (fabricated by OT)	T1: 2-5 days T2: 2 weeks T3: 4-6 weeks	Patient satisfaction Production time Adverse events	Questionnaires Recorded mins Number of events	Overall 8.4 ± 1.65 (EA) vs 9.2 ± 1.32 (CG); Splint fit 9.15 ± 1.11 vs 9.2 ± 0.79 517 min (279-1077) vs 39.5 min (30-60) 1/14 vs 0/10, ns
Wang et al., 2018 (China)	Time-series study (NCCT)	18 I	Hand spasm secondary to stroke	Static volar 3D-printed HFO (3 months) *PLA*	T1: 3 weeks T2: 3 months	Reduction in pain Grip-strength improvement ROM improvement Spasticity reduction Hand-function improvement	VAS GSI Fingertip-to-palm and wrist ROM MAS Brunnstrom approach	2.0±1.58 (T0), 1.85±1.34 (T1), 1.69±1.03 (T2) 0.018±0.041 (T0), 0.025±0.054 (T1), 0.032±0.067 (T2) Fingertip to palmprint: Δ(T1-T0): -1.7 mm, -12% (active) and -2.0 mm, -33% (passive); Δ(T2-T0): -2.6 mm, -18% (active) and -2.3 mm, -37% (passive); Wrist flexors: Δ(T1-T0): +2.25°, +94% (active) and +4°, +9.7% (passive); Δ(T2-T0): +3.2°, +123% (active) and +3.8°, +9.2% (passive); Wrist extensors: Δ(T1-T0): +2.6°, +262% (active) and +2.9°, +8.2% (passive); Δ(T2-T0): +2.9°, +285% (active) and +4.3°, +12% (passive) 2.38±0.63 — 2.31±0.48 — 1.73±0.69, p<0.05 2.77±0.80 — 3.00±0.78 — 3.31±0.77, p<0.05

(continue)

First author, year (country)	*Study design*	*Subject N (I, C)*	*Diagnosis*	*Intervention and comparator orthosis type (and wearing time) Material of customization*	*Baseline and follow up*	*Outcomes*	*Method*	*Main results*
Yoo et al., 2019 (South Korea)	Before-&-After study (NCCT)	10 I	Cervical spinal-cord injury (chronic)	Dynamic 3D-printed myoelectric WHFO *PLA* C: Non-use of orthosis	NA	Improvement in hand function	TRI-HFT (I & II)	TRI-HFT I: 29.4 → 45.0; II: 26.8 → 47.6 ($p < 0.01$)
						Improvement in ADL	FIM; SCIM III	FIM 11.3 → 13.4; SCIM III 4.6 → 6.1
						Patient satisfaction	QUEST 2.0	QUEST: Dim 3.2; Weight 3.8; Comfort 3.8; Effectiveness 4.5
Zheng et al., 2020 (China)	RCT	20 I 20 C	Wrist-flexor spasticity (chronic post-stroke)	Static circular 3D-printed WHO (6 weeks, 4-8 hours/day) I: *Light-activated resin* C: *Low-temp thermoplastic* (volar WHFO)	T1: 3 weeks T2: 6 weeks	Spasticity reduction	MAS	↓ ≥1 MAS point in 65 % (EA) vs 30 % (CG), $p = 0.02$
						ROM improvement	PROM (ext/flex + radial/ulnar dev.)	Wrist ext +10.3° vs +3.3° ($p < 0.001$); ulnar dev +5.3° vs +1.1°
						Motor-function improvement	FMA	+1.3 vs +0.2 ($p < 0.001$)
						Pain reduction	VAS	Pain: no significant change
						Patient satisfaction	QUEST (18 items using 5-point scale)	QUEST 67.9 ± 6.7 vs 64.3 ± 11.8, n.s.
						Swelling	Swelling score (0-3)	↓1.5 vs 0, $p < 0.001$

Table 1. *Main characteristics of the studies. Abbreviations: C: Comparators, FMA: Fugl-Meyer Assessment, FIM: Function Indipendence Measure, GSI: Grip Strength Index (Kg/Kg x100), HFO: Hand-Finger Orthosis, I: Intervention group, JHFT: Jebsen Hand Function Test, MAS: Modified Ashworth Score, NA: not applicable, NCCT: Non-Controlled Clinical Trial, OT: Occupational Therapist, PLA: polylactic*

*plastic, PRWE: Patient-Rated Wrist Evaluation, QUEST: Quebec User Evaluation of Satisfaction with assistive Technology, RCT: Randomized Clinical Trial, ROM: Range Of Motion, SCIM: Spinal Cord Independence Measure, TRI-HFT: Toronto Rehabilitation Institute Hand Function Test, VAS: Visual Analogue Scale. *3D-printed orthoses (additive manufacturing), WHO: Wrist-Hand Orthosis, WHFO: Wrist-Hand-Finger Orthosis*

RoB 2 domain	Gwilym et al, 2020	Martynov et al, 2020	Waldburger et al, 2021	Zheng et al, 2020
Bias arising from the randomisation process	**Low risk** Central computer system with variable block sizes, stratified by site & age; allocation concealed from recruiters until after consent.	**Low risk** Computer-generated list, block randomisation, age/sex stratification, concealed in sealed opaque envelopes; baseline groups well balanced.	**Some concerns** Group allocation by "envelope draw", but sequence generation method and envelope preparation not reported; very small pilot sample (n = 20) increases unpredictability.	**Low risk** 1:1 computer-generated table with consecutively numbered, sealed opaque envelopes; randomisation overseen by an independent researcher; baseline comparability adequate.
Bias due to deviations from intended interventions *(effect of assignment)*	**Some concerns** Open-label design; primary outcomes include self-reported pain and PRWE scores could be affected by expectations.	**Some concerns** Open-label (participants, clinicians, research staff not blinded). Primary endpoint is objective but several subjective satisfaction outcomes could have been influenced by knowledge of group. No evidence of protocolised co-interventions and analysis was ITT.	**Some concerns** Blinding judged "not feasible"; patient-reported comfort is highly prone to expectation effects; no indication that analyses corrected for any non-adherence.	**Low risk** Outcome assessor remained blinded to allocation throughout; treatments delivered per protocol and no deviations that were likely to bias results were described.
Bias due to missing outcome data	**Some concerns** 83 % provided 3-month outcomes; >10 % attrition and imbalance could bias estimates.	**Low risk** 98.8 % contributed to the primary endpoint and 76.5 % completed all visits; reasons for loss were balanced and ITT analysis used.	**Low risk** 20/24 randomised completed all assessments; four early drop-outs were replaced leaving complete data for final analysis (pilot feasibility aim).	**Low risk** 40/44 randomised patients (91 %) analysed; losses (n=4) were unrelated to treatment and balanced between groups.
Bias in measurement of the outcome	**Some concerns** Outcomes are subjective; no assessor blinding in an open-label trial.	**Some concerns** Objective breakage data unlikely to be influenced, but satisfaction ratings collected by unblinded staff; no blinding of participants.	**High risk** All outcomes were self-reported comfort/satisfaction, collected by unblinded therapists in a non-masked setting.	**Low risk** Primary outcome measured by a single blinded assessor; scale has established reliability; identical assessment schedule for both arms.

Bias in selection of the reported result	**Some concerns** Feasibility trial reported many outcomes but lacked a prespecified hierarchy; no publicly available protocol.	**Some concerns** No published protocol or statistical analysis plan; exploratory design increases risk of selective emphasis, although all prespecified outcomes appear to be reported.	**Some concerns** Pilot study without pre-registered protocol; reporting focused mainly on feasibility metrics; small sample may prompt selective emphasis of favourable findings.	**Some concerns** Registered trial but it did not detail all secondary outcomes; manuscript reports a wide range of scales – risk of selective emphasis cannot be excluded.
Overall judgement	**Some concerns**	**Some concerns**	**High risk**	**Low risk**

Table 2. *RoB2 Assessment for RCTs.*

Study	*Clear question*	*Eligibility prespecified*	*Representative/ consecutive sample*	*Sample-size justified*	*Intervention clearly described*	*Outcome measures valid & reliable*	*≥ 2 time-points (pre / post)*	*Outcome assessor blinded*	*Follow-up complete / attrition handled*	*Stats appropriate*	*Baseline comparable or adjusted*	*Confounders measured / adjusted*	*Overall quality*
Chae et al, 2020	Y	NR	N	N	Y	Y	Y	N	Y	CD	N	N	***Poor***
Chang et al, 2018	Y	NA	NA	N	Y	CD	Y	N	NA	CD	NA	N	***Poor***
Lindsfors & Salo, 2012	Y	NR	CD	N	Y	NR	Y	N	Y	CD	N	N	***Fair***
Lindsfors & Salo, 2014	Y	Y	Y	N	Y	NR	Y	N	Y	CD	N	N	***Fair***
Portnova et al, 2018	Y	NR	N	N	Y	CD	Y	N	NA	CD	NA	N	***Poor***
van der Stelt et al, 2020	Y	Y	CD	N	Y	CD	Y	N	**Y**	CD	CD	N	***Fair***
Wang et al, 2016	Y	Y	Y	N	Y	Y	Y	N	CD	CD	CD	N	***Fair***
Yoon et al, 2019	Y	Y	CD	N	Y	Y	Y	N	Y	Y	CD	N	***Fair***

Table 3. *NIH Quality Assessment of Non-Controlled Clinical Trials. Abbreviations: Y: Yes; N: No; CD: Cannot determine; NR: Not reported; NA: Not Applicable.*

Figures

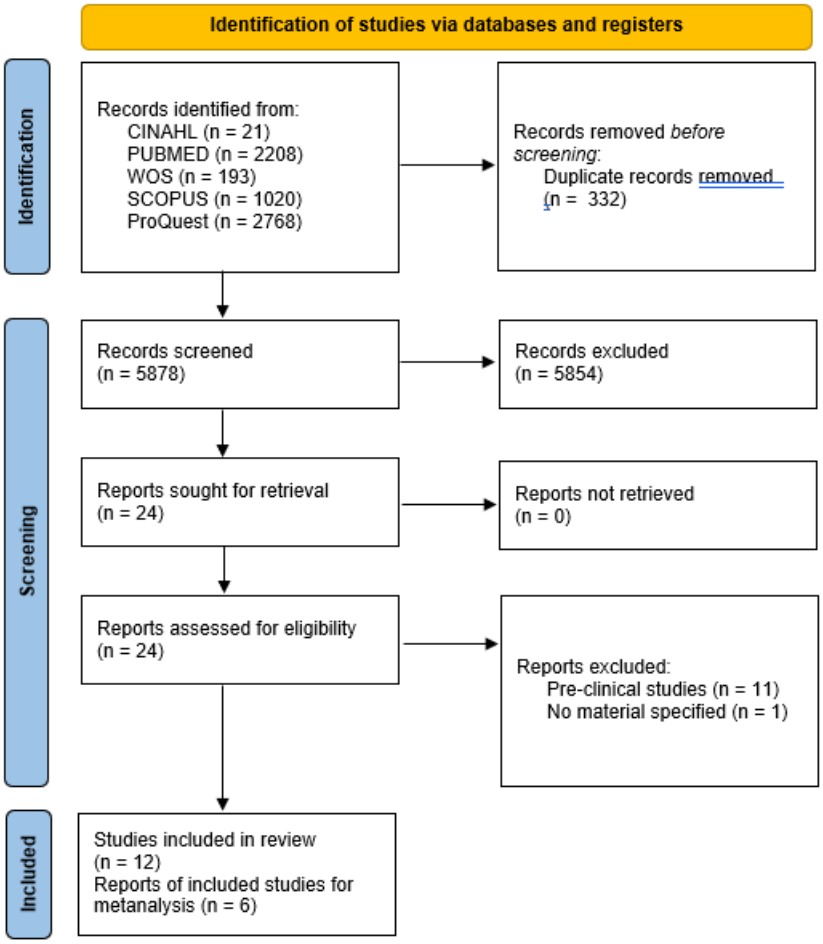

Figure 1. *PRISMA flow-chart of the included study*

Figure 2. *RoB2 Tool for quality assessment of RCTs.*

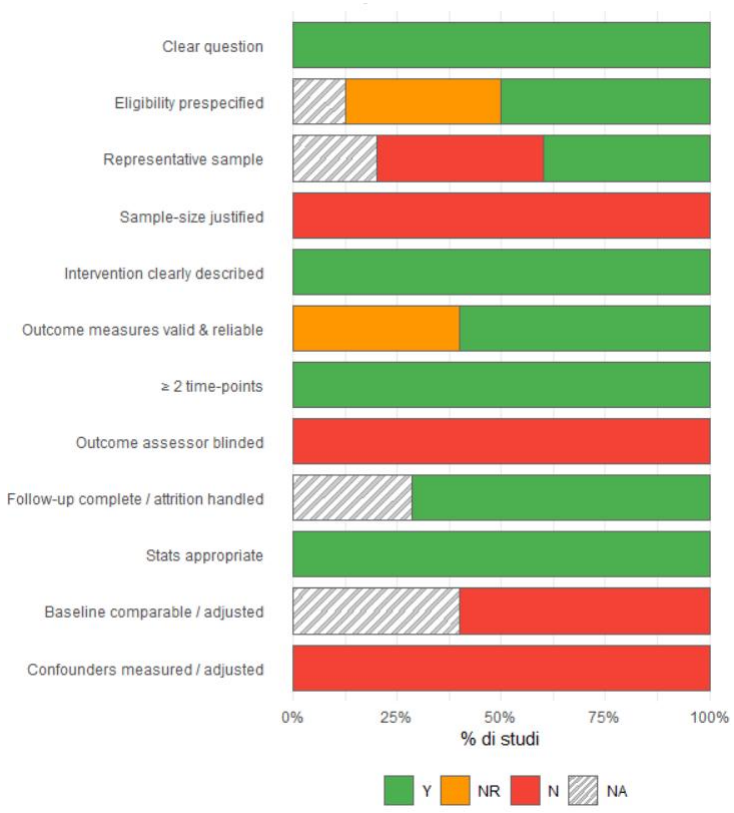

Figure 3. *NIH quality assessment for NCCTs.*

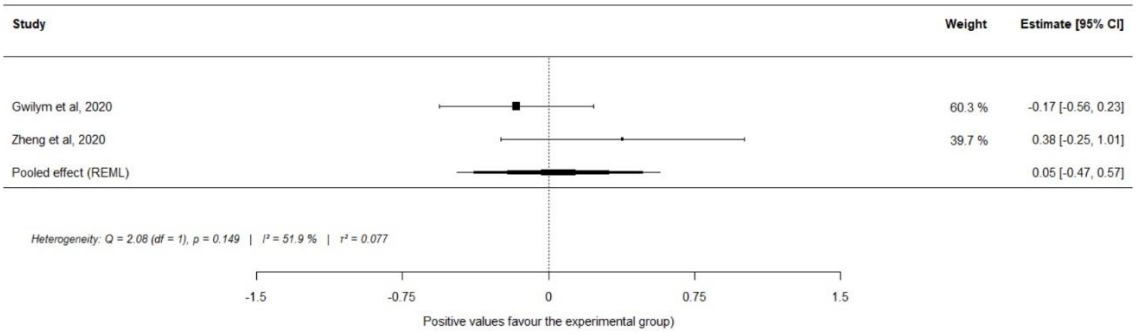

Figure 4. *Forest plot of improvement in hand functionality (positive values favour the experimental device).*

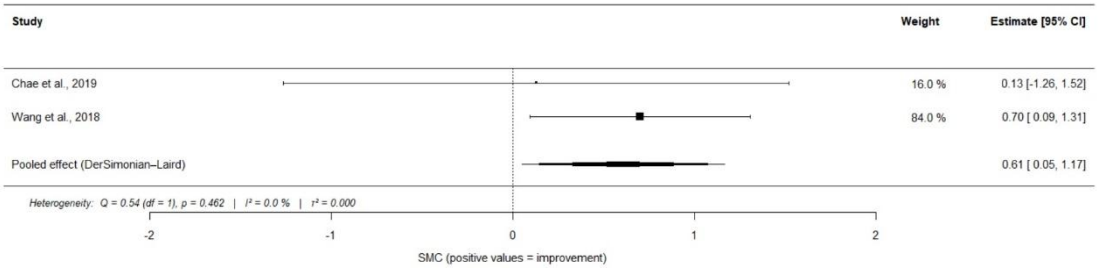

Figure 5. *Single-arm forest plot of SMC (standardised mean change, Hedges-corrected) within each study, where positive values indicate post-treatment improvement in hand function.*

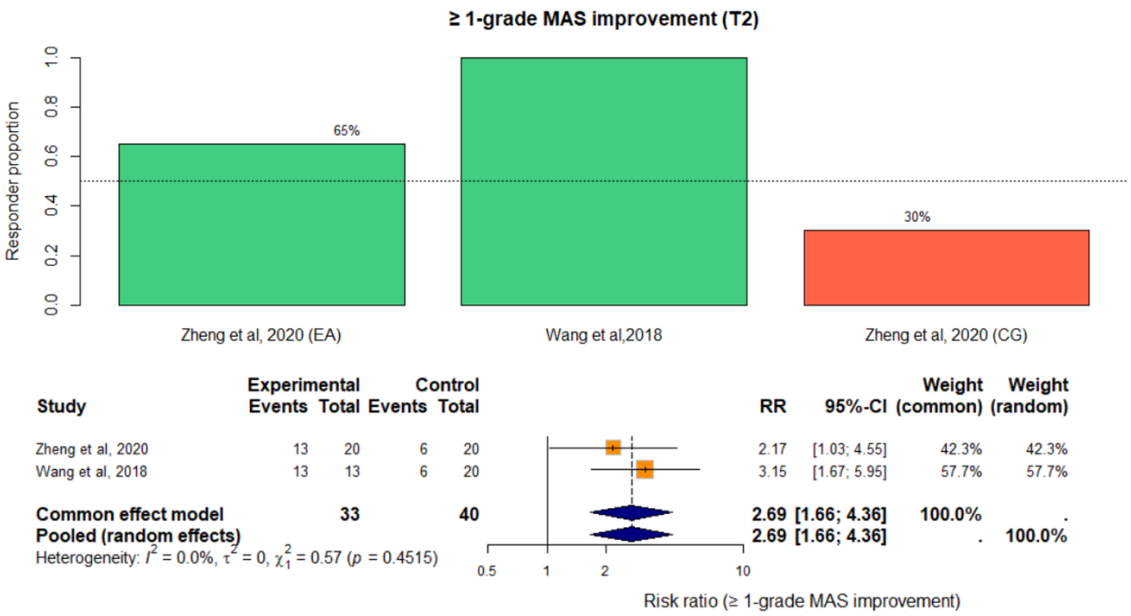

Figure 6. A) *Proportion of responders. The bar chart displays the percentage of participants who achieved at least a 1-grade reduction on the Modified Ashworth Scale at the final follow-up (T2).* ***B)*** *Meta-analysis of risk ratios. The forest plot summarises the comparative effectiveness of biodegradable versus conventional orthoses in producing a ≥ 1-grade MAS improvement.*

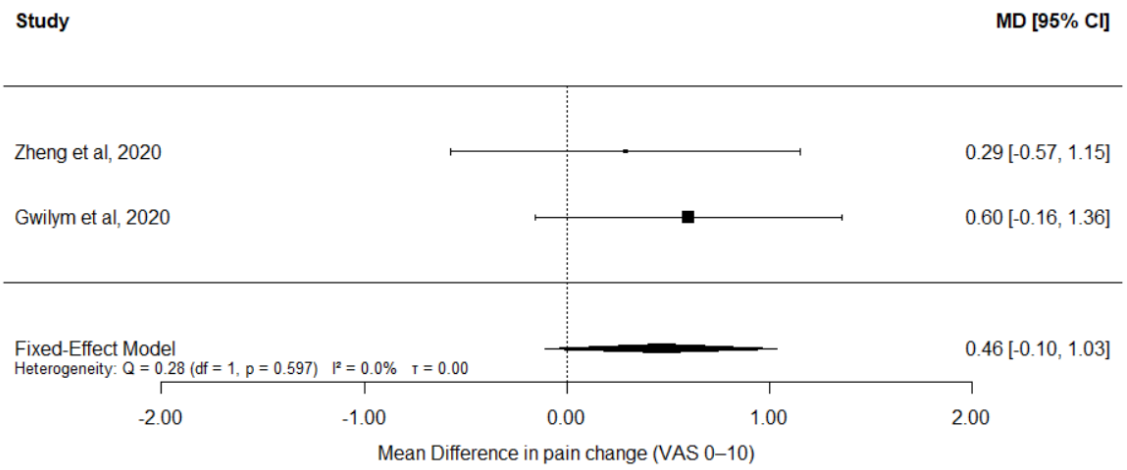

Figure 7. *Forest plot of mean pain change differences (negative values indicate greater pain reduction with the biocomposite orthosis). Studies' weight: 43.85% for Zheng, 2020 and 56.15% for Gwilym.*

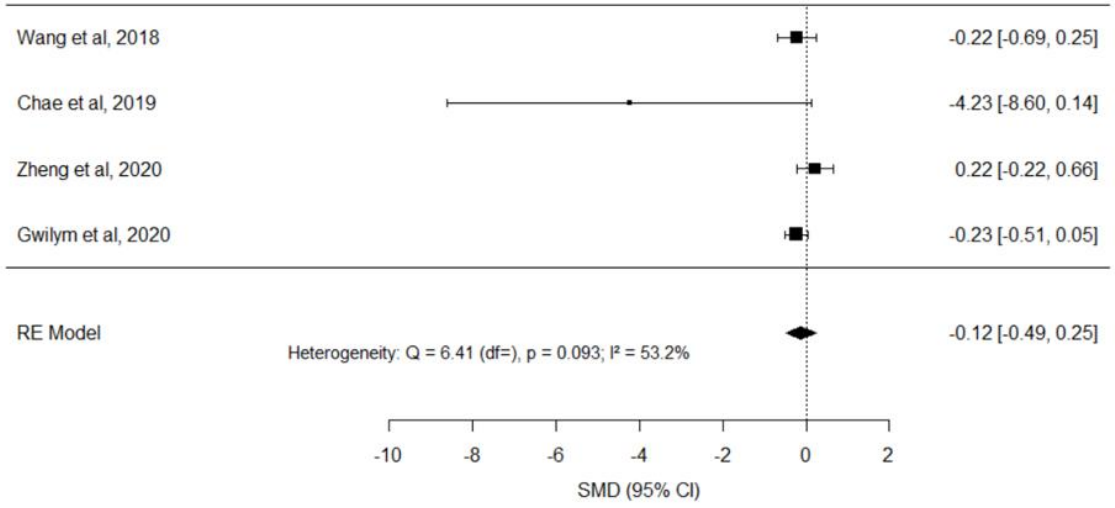

Figure 8. *Forest plot of Hedges g for pain change after treatment with biocomposite orthoses. Negative values favour pain. Studies' weight: 0.65% for Chae, 45.55% for Gwilym, 25.98% for Wang, 27.83% for Zheng.*

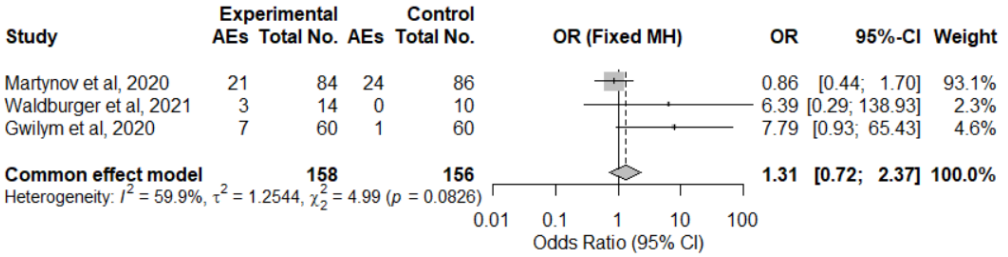

Figure 9. *Forest plot of fixed-effect Mantel–Haenszel ORs for device-related adverse events with bio-derived versus conventional materials.*

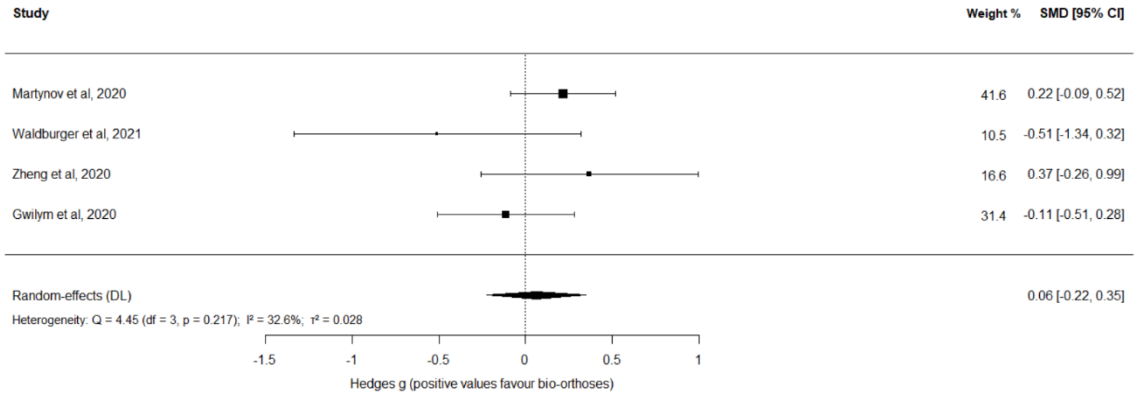

Figure 10. *Forest plot of patient-satisfaction outcomes comparing bio-based orthoses with conventional materials. Values to the right indicate greater satisfaction with the experimental orthoses materials.*

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